REMARKS

I. Detailed Action

A. Continued Examination Under 37 C.F.R. § 1.144

Applicant acknowledges that a request for continued examination under 37 C.F.R. § 1.144 has been entered. Applicant further acknowledges that since this application is eligible for continued examination under 37 C.F.R. § 1.144 and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 C.F.R. § 1.144 and prosecution in this application has been reopened pursuant to 37 C.F.R. § 1.144. Applicant additionally acknowledges that the Examiner has acknowledged Applicant's amendment filed on January 20, 2004.

B. Declaration

Applicant acknowledges that the Examiner has acknowledged and fully considered the declaration by William E. Marshall filed under 37 C.F.R. § 1.132.

C. Claim Rejections Withdrawn

Applicant acknowledges that the rejection of claim 12 under 35 U.S.C. § 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "stress response factors (SRFs) <10kDa" is withdrawn in light of the amendment thereto.

II. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 1, 4-8 and 10-16 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claims the subject matter which application regards as the invention.

Specifically, claims 1 and 17-19 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner states claims 17-19 are vague and indefinite due to the phrase "sequential periods of stress" as it is unclear what is meant by the phrase.

Applicant respectfully traverses this rejection. The Examiner states that Applicant has defined what constitutes a period of stress. As taught by the specification, "sequential periods of stress" are said defined periods of stress performed in succession:

> A convenient means of sequential stressing is to transfer the bacteria from their growth medium into fresh PBS. This transfer is marked by the immediate release of SRFs. Transferring the bacteria into fresh PBS again induces the release of additional SRFs (specification, page 12).

What demarcates the end of one period and the onset of the next is therefore defined by what constitutes a period. The initial period of stress is defined by the time period which the bacteria are exposed to stress. When the stress exposure is concluded, the initial stress period is over. The successive stress period then begins when the bacteria are exposed to a fresh period of stress. As taught by the Applicant, bacteria exposed to sequential periods of stress for shorter periods of time yield more effective and potent SRFs. The preferred stress period is 20 minutes, although SRFs are released during stress periods as short as 10 minutes (specification, page 12).

The specification further teaches that there are multiple ways in which sequential stressing may be performed (specification, page 12). A specific example of successive stressing is taught in Example 13 (specification, page 25). In Example 13, the stress factors released and recovered from each period were labeled as A, B, and C and the results from each are shown in Table 9. Monocytes or mice were administered either the A, B or C SRFs, resulting in different percentages of survival (specification, pages 25, 27-28).

In an effort to expedite prosecution Applicant has amended claim 18, thereby further defining the phrase "sequential periods of stress" by clearly stating the beginning and end of the sequential periods. Therefore, Applicant asserts that claims 1 and 17-19 as amended are not indefinite and would be understood by one skilled in the art. Applicant respectfully requests reconsideration.

Claims 4-5 stand rejected as being vague and indefinite as being dependent on a canceled claim.

Applicant has amended claim 4 to properly depend from claim 1, thereby alleviating this rejection.

Claim 1 stands rejected as being rendered vague and indefinite by the use of the phrase "activating and modulating" as it is unclear what is meant by said phrase.

Applicant respectfully traverses this rejection. The specification teaches separate and distinct meanings of the terms activating and modulating.

Bacteria, upon encountering regular forms of stress, release natural products known as SRFs. The bacterial host is alerted to the presence of the bacteria by the SRFs, causing the activation of the appropriate immune response in the host (specification, page 2). On a cellular level, this involves the activation of macrophages. As taught by the specification:

> Specifically, the macrophage has adapted a pre-emptory reaction to the presence of the SRFs that prepares the immune system to defend the host against infection. For example, when commensal bacteria are overcrowded by the presence of growing pathogens, they will release readily absorbable, non-toxic SRFs which activate tissue macrophages to release Interleukin-1, IL-1, Interleukin-6, IL-6 and Tumor Necrosis Factor, alpha, TNFα which stimulate other cells of the immune system (specification, page 3).

The present invention in part relates to the stimulation of an animal's immune system by "activating macrophages to release cytokines, in particular IL-1, IL-6 and TNF required to initiate an immune response to prevent or reduce infection" (specification, page 10). Activating is therefore defined as the release of cytokines by macrophages in order to stimulate the proper immune response in an animal.

Modulating, which is distinct from activating, is defined on a cellular level as the down-regulation of macrophage receptors to prevent their over-stimulation by (1) endotoxin, which leads to systemic inflammation, cardiovascular dysfunction, shock, or death, as well as (2) IL-10, which leads to the potentially excessive self-destruction of cells (specification, page 10). Modulating also involves rescuing monocytes from apoptosis (specification, page 10). The specification teaches that the SRFs of the present invention act as immune system modulators by protecting against over-stimulation of the immune system (specification, page 5). Modulating is thus defined as the regulation of macrophage receptors so as to prevent their over-stimulation and any resulting negative effects. This is a separate and distinct definition than that of "activating". Therefore, Applicant asserts that claim 1 is not indefinite and would be understood by one skilled in the art. Applicant respectfully requests reconsideration.

In light of the above amendment and remarks, Applicant asserts the claims are now in a condition for allowance. Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

III. Claim Rejections – 35 U.S.C. § 103(a)

Claim Rejections - 35 U.S.C. 103 over De Vuyst et al.:

Claims 1, 4-8 and 10-19 remain rejected under 35 U.S.C. § 103(a) as obvious over De Vuyst *et al.* as the Examiner states that De Vuyst *et al.* suggests that low molecular weight proteins (bacteriocins) are produced by stressed bacteria.

Applicant respectfully traverses this rejection. All of the claim elements must be taught or suggested by the combined references. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). De Vuyst *et al.* does not teach the use of factors other than bacteriocins for stimulation of the immune system upon administration. As disclosed by the March 17, 2003 37 C.F.R. § 1.132 declaration of William E. Marshall, the stress response factors (SRFs) of the present invention do not include bacteriocins. Rather, they are composed of a mixture of 10-13 oligoribonucleotides, containing from 1 to 5 nucleotides plus the base uracil.

Applicant has amended claim 1 to include the phrase -- wherein said SRFs are not bactericidal proteins or peptides --, thereby further defining the phrase SRFs. According to the Examiner, De Vuyst *et al.* would have made obvious to one skilled in the art at the time the invention was made the administration of low molecular weight *proteins* produced by stressed bacteria. Since Applicant's amendment has made it clear that the SRFs of the present invention do not include bactericidal proteins, and De Vuyst *et al.* does not teach the administration of non-bacteriocin SRFs, Applicant respectfully requests that this ground of rejection be withdrawn.

Claim Rejections - 35 U.S.C. 103(a) over De Vuyst et al. in view of Nanji:

Claims 1, 4-8, 10-15, and 17-19 remain rejected under 35 U.S.C. § 103(a) as obvious over De Vuyst *et al.* in view of Nanji as the Examiner states the cited references disclose the administration of lactic acid bacteria to animals for protection against endotoxin-mediated shock.

Applicant respectfully traverses this rejection. As stated *supra*, De Vuyst *et al.* does not teach the use of factors other than bacteriocins for stimulation of the immune system upon administration. Nanji discloses administering lactic acid bacteria to reduce the quantity of endotoxin within a mammal's blood plasma and that said bacteria should be able to produce proteinaceous antagonistic substances (bacteriocins). Neither reference teaches that SRFs other than bacteriocins may be administered to a mammal in order to modulate its immune system.

As stated *supra*, Applicant has amended claim 1 so as to define SRFs as not including bacteriocidal proteins or peptides. According to the Examiner, it would have been obvious to one skilled in the art to use the *bacteriocins* disclosed in De Vuyst *et al.* in the treatment methodologies of Nanji. However, neither De Vuyst *et al.* or Nanji, alone or in combination, teach the critical claim limitation of administering non-bacteriocin SRFs. Applicant therefore respectfully requests that this ground of rejection be withdrawn.

Claim Rejections - 35 U.S.C. 103(a) over De Vuyst et al. in view of Perdigon et al.:

Claim 16 remains rejected under 35 U.S.C. § 103(a) as obvious over De Vuyst *et al.* in view of Perdigon *et al.* as the Examiner states that Perdigon discloses the use of low molecular weight proteins as adjuvants.

Applicant respectfully traverses this rejection. As stated *supra*, De Vuyst *et al.* does not teach the use of factors other than bacteriocins for stimulation of the immune system upon administration. Perdigon *et al.* discloses the use of proteins produced by lactic acid bacteria as adjuvants in order to protect from enteropathogens. Neither reference teaches that SRFs other than bacteriocins may be administered to a mammal in order to modulate its immune system.

As stated *supra*, Applicant has amended claim 1 so as to further define SRFs as not including bacteriocidal proteins or peptides. According to the Examiner, it would have been obvious to one skilled in the art to use the bacteriocidal proteins disclosed by De Vuyst *et al.* as adjuvants for enteropathogens as disclosed by Perdigon *et al.* Neither De Vuyst *et al.* or Perdigon *et al.*, alone or in combination, teach the critical claim limitation of administering non-bacteriocin SRFs. Applicant therefore respectfully requests that this ground of rejection be withdrawn.

III. Conclusion

In light of the above amendments and remarks, Applicant asserts that the claims as amended are in condition for allowance. Applicant respectfully requests reconsideration and withdrawal of the above rejections to claims 1, 4-8 and 10-19. If it is felt that it would aid in prosecution, the Examiner is invited to contact the undersigned at the number indicated to discuss any outstanding issues.

No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any fees inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

LILA A. T. AKRAD, Reg. No. 52,550
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338
CUSTOMER NO: 22885

Attorneys of Record

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